

*Study Title*  
COMBINED CHRONIC TOXICITY/ONCOGENICITY  
STUDY 2-YEAR ORAL GAVAGE STUDY IN RATS

Laboratory Project ID:

**Volume 10 of 13**

**NUMBER OF PAGES IN VOLUME:** 351

- TEST GUIDELINES:**
- U.S. EPA Health Effects Test Guidelines OPPTS 870.4300 Combined Chronic Toxicity/Carcinogenicity (1998)
  - OECD Guidelines for the Testing of Chemicals Section 4 (No. 453) Health Effects (2009)
  - JMAFF Japan Agricultural Chemicals Regulation Law 12 Nousan No. 8147 (2000)
  - EEC Methods for the Determination of Toxicity Method B.33 Combined Chronic/Carcinogenicity test, Directive 88/302/EC (1988)

**AUTHOR:**

**STUDY COMPLETED ON:** March 28, 2013

**APPLICANT/SPONSOR:**

**PERFORMING LABORATORY:**

**WORK REQUEST NUMBER:**

**SERVICE CODE NUMBER:**

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1318	E	<b>Microscopic</b> salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea	- within normal limits - within normal limits - within normal limits - hyperplasia, epidermal, mild corresponds to macroscopic observation (skin - abrasion/scab) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - astrocytoma, malignant, primary, fatal, positive cause of death - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u>			
1318	E	<b>Microscopic</b> ureters urinary bladder Cause of Death	- within normal limits - within normal limits - spinal cord tumor
1319	S	<b>Macroscopic</b> lymph node, inguinal  skin, subcutis  testes	- not identified, right, no grade draining node for mass a. - mass, tan, mass a, right inguinal area, present corresponds to antemortem observation (nodule) approximately 0.5 cm in diameter. - discoloration, red, right, moderate
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1319	S	<b>Microscopic</b> adrenal glands	<ul style="list-style-type: none"> <li>- hyperplasia, focal cortical, unilateral, minimal</li> <li>- hyperplasia, focal medullary, unilateral, mild</li> <li>- necrosis, unilateral, mild</li> <li>- vacuolation, focal, unilateral, minimal</li> </ul> <p>two sets of adrenals submitted with this animal from necropsy. one set has only medullary hyperplasia.</p>
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		coagulating glands	- within normal limits
		epididymides	- oligospermia/germ cell debris, unilateral, severe
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1319	S	<b>Microscopic</b> harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b	- within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1319	S	<b>Microscopic</b> nose, level c nose, level d pancreas  parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum	- within normal limits - within normal limits - adenoma, acinar cell, benign, primary, incidental, not cause of death - hyperplasia, acinar cell, focal, mild - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits

S - Scheduled necropsy

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1319	S	<b>Microscopic</b> small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes  thymus  thyroid gland tongue trachea	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, interstitial cell, benign, unilateral, primary, incidental, not cause of death corresponds to macroscopic observation (testes - discoloration, red) - hyperplasia, interstitial cell, unilateral, minimal - depletion, lymphoid, generalized, severe two sets of thymus submitted from necropsy. both have same microscopic finding. - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u>			
1319	S	<b>Microscopic</b> ureters urinary bladder	- within normal limits - within normal limits
1320	E	<b>Macroscopic</b> pituitary gland stomach, nonglandular	- enlarged, moderate - swollen/thickened, mild
1320	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1320	E	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1320	E	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum	- within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, acinar cell, focal, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>50 mg/kg/day</u> 1320	E	<b>Microscopic</b> small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - erosion/ulcer, severe corresponds to macroscopic observation (stomach, nonglandular - swollen/thickened) - hyperplasia, interstitial cell, bilateral, minimal - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1321	D	<b>Macroscopic</b> pituitary gland	- enlarged, minimal
1321	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- not examined
			autolysis too severe for diagnosis
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1321	D	<b>Microscopic</b> joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - histiocytosis, alveolar, minimal - within normal limits - within normal limits - hyperplasia, lobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

## Terminal

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D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1321	D	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina non-correlated macro observation Cause of Death	- depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary gland - enlarged - undetermined
1323	D	<b>Macroscopic</b> all tissues	- within normal limits
1323	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur	- within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1323	D	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, tubular, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1323	D	<b>Microscopic</b> liver lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx pituitary gland salivary gland, mandibular salivary gland, parotid	- infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - hyperplasia, lobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1323	D	<b>Microscopic</b> salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1323	D	<b>Microscopic</b> vagina Cause of Death	- within normal limits - undetermined
1333	S	<b>Macroscopic</b> ovaries pituitary gland uterus with cervix	- cyst, clear, right, mild - enlarged, red, severe - enlarged, horn, mild
1333	S	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits
S - Scheduled necropsy D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1333	S	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1333	S	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, primary, incidental, not cause of death slide 18.
		nerve, sciatic	- hyperplasia, lobular, mild
		nose, level a	- degeneration, axonal/myelin, minimal
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- hyperplasia, sex-cord/stromal, unilateral, mild
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
			one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
			corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1333	S	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland  tongue trachea ureters	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1333	S	<b>Microscopic</b> urinary bladder uterus with cervix	- within normal limits - dilatation, gland/lumen, moderate corresponds to macroscopic observation (uterus with cervix - enlarged)
		vagina non-correlated macro observation	- within normal limits - ovaries - cyst
1334	E	<b>Macroscopic</b> adrenal glands lymph node, axillary	- enlarged, right, mild - within normal limits draining node for mass a and mass b, left. draining node for mass e, right.
		lymph node, inguinal pituitary gland	- within normal limits draining node for mass c, left. draining node for mass d, right. - enlarged, red, moderate

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1334	E	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, left axillary area, present corresponds to antemortem observation (mass 1) approximately 4.5 cm in diameter.</li> <li>- mass, tan, mass b, left axillary area, present corresponds to antemortem observation (mass 2) approximately 2.5 cm in diameter.</li> <li>- mass, tan, mass c, left anogenital region, present corresponds to antemortem observation (mass 3) approximately 4.7 cm in diameter.</li> <li>- mass, tan, mass d, right anogenital region, present corresponds to antemortem observation (mass 4) approximately 4.0 cm in diameter.</li> <li>- mass, tan, mass e, right axillary area, present corresponds to antemortem observation (mass 5) approximately 1.9 cm in diameter.</li> </ul>
1334	E	<b>Microscopic</b> adrenal glands	<ul style="list-style-type: none"> <li>- angiectasis/cystic degeneration, focal cortical, bilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged)</li> <li>- hyperplasia, focal cortical, unilateral, mild</li> </ul>

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1334	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1334	E	<b>Microscopic</b> large intestine, rectum larynx liver  lung lymph node, axillary lymph node, inguinal lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - hyperplasia, bile duct, minimal - vacuolation, periportal, mild - within normal limits - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1334	E	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b; skin, subcutis - mass c; skin, subcutis - mass d; skin, subcutis - mass e) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1334	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters	- within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1334	E	<b>Microscopic</b> urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - pituitary tumor
1335	S	<b>Macroscopic</b> liver lymph node, inguinal  lymph node, mesenteric  pancreas	- cyst, clear, left lateral lobe, moderate - not identified, bilateral, no grade draining node for mass a, right and mass b, left. - within normal limits draining node for mass c. - mass, tan, mass c, present approximately 1.0 cm in diameter.

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1335	S	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, right anogenital region, present corresponds to antemortem observation (hair sparse mass 1) approximately 9.0 x 8.0 x 3.2 cm.</li> <li>- mass, tan, mass b, left inguinal area, present corresponds to antemortem observation (mass 2) approximately 4.0 x 4.0 x 3.5 cm.</li> </ul>
1335	S	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina	<ul style="list-style-type: none"> <li>- angiectasis/cystic degeneration, focal cortical, bilateral, mild</li> <li>- within normal limits</li> <li>- hyperplasia, granulocytic, mild</li> <li>- hyperplasia, granulocytic, minimal</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> </ul>
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1335	S	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, unilateral, minimal - pyelitis, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cyst, biliary, simple, mild corresponds to macroscopic observation (liver - cyst) - focus of cellular alteration, basophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - histiocytosis, alveolar, minimal - macrophages, pigmented alveolar, minimal
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1335	S	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas  parathyroid glands	- within normal limits - within normal limits - fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, sex-cord/stromal, unilateral, mild - within normal limits - atrophy, acinar, minimal - carcinoma, islet cell, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (pancreas - mass c) - within normal limits one of pair present
S - Scheduled necropsy			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1335	S	<b>Microscopic</b> pharynx pituitary gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland	- within normal limits - hyperplasia, focal, pars distalis, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1335	S	<b>Microscopic</b> tongue trachea ureters urinary bladder uterus with cervix vagina	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
1336	E	<b>Macroscopic</b> lymph node, axillary  lymph node, inguinal  pituitary gland	- within normal limits draining node for mass b, left and mass d, right. - not identified, bilateral, no grade draining node for mass a, right and mass c, left. - enlarged, red, severe

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1336	E	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, right anogenital region, present corresponds to antemortem observation (hair sparse mass 1) approximately 10.0 x 5.5 x 3.5 cm.</li> <li>- mass, tan, mass b, left axillary area, present corresponds to antemortem observation (mass 2) approximately 6.5 x 5.0 x 3.0 cm.</li> <li>- mass, tan, mass c, right inguinal area, present corresponds to antemortem observation (mass 3) approximately 3.0 cm in diameter.</li> <li>- mass, tan, mass d, right axillary area, present approximately 1.0 cm in diameter.</li> <li>- small, severe</li> </ul>
1336	E	thymus <b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur	<ul style="list-style-type: none"> <li>- angiectasis/cystic degeneration, focal cortical, bilateral, mild</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1336	E	<b>Microscopic</b> bone, sternum brain  esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	- within normal limits - carcinoma, pars distalis, malignant, secondary - compression, ventral (pituitary tumor), moderate - hemorrhage, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1336	E	<b>Microscopic</b> liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland   nerve, sciatic nose, level a nose, level b	<ul style="list-style-type: none"> <li>- focus of cellular alteration, basophilic, minimal</li> <li>- hyperplasia, bile duct, minimal</li> <li>- histiocytosis, alveolar, minimal</li> <li>- within normal limits</li> <li>- erythrocytosis/erythrophagocytosis, sinus, minimal</li> <li>- within normal limits</li> <li>- adenocarcinoma, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (skin, subcutis - mass d)</li> <li>- adenoma, benign, primary, incidental, not cause of death slide 18.</li> <li>- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b; skin, subcutis - mass c)</li> <li>- hyperplasia, lobular, moderate</li> <li>- degeneration, axonal/myelin, minimal</li> <li>- within normal limits</li> <li>- degeneration, mild squamous epithelium, oral mucosa.</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1336	E	<b>Microscopic</b> nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum	- within normal limits - within normal limits - cyst, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, pars distalis, malignant, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1336	E	<b>Microscopic</b> spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate corresponds to macroscopic observation (thymus - small) - hyperplasia, epithelial cell, minimal - hyperplasia, c-cell, focal, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1337	E	<b>Macroscopic</b> animal/whole body	- body fat depleted, mild corresponds to antemortem observation (thin)
		liver	- discoloration, tan, multiple lobes, mild
		lung with bronchi	- mass, tan, multiple, multiple lobes, mass b, present ranging in size from approximately 0.2 to 2.0 cm in diameter.
		lymph node, mandibular	- discoloration, red, bilateral, mild draining node for mass a.
		lymph node, mediastinal	- not identified, no grade draining node for mass b.
		skin, subcutis	- mass, tan, mass a, ventral neck, present corresponds to antemortem observation (mass 1) approximately 12.0 cm in diameter.
1337	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1337	E	<b>Microscopic</b> bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, unilateral, minimal - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, mild  - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1337	E	<b>Microscopic</b> liver	- vacuolation, periportal, mild corresponds to macroscopic observation (liver - discoloration, tan)
		lung	- adenocarcinoma, malignant, secondary corresponds to macroscopic observation (lung with bronchi - mass b)
		lymph node, mandibular	- erythrocytosis/erythrophagocytosis, sinus, mild corresponds to macroscopic observation (lymph node, mandibular - discoloration, red)
		lymph node, mesenteric	- within normal limits
		mammary gland	- adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits

E - Euthanized *in extremis*

## Terminal

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1337	E	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mammary tumor
1338	E	<b>Macroscopic</b> lymph node, axillary  pituitary gland	- within normal limits draining node for mass a, left, and mass b, right. - enlarged, tan, moderate

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1338	E	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, left axillary area, present corresponds to antemortem observation (mass 1) approximately 3.0 x 2.5 x 1.5 cm.</li> <li>- mass, ulcerated, mass b, right axillary area, present corresponds to antemortem observation (mass 2) approximately 2.5 x 2.0 x 1.5 cm, tan, possible cannibalism.</li> </ul>
1338	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves	<ul style="list-style-type: none"> <li>- angiectasis/cystic degeneration, focal cortical, bilateral, mild</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- compression, ventral (pituitary tumor), mild</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- one of pair present</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1338	E	<b>Microscopic</b> eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, clear, minimal - hematopoiesis, extramedullary, minimal - infiltration, mononuclear cell, minimal - necrosis, focal, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1338	E	<b>Microscopic</b> lymph node, mesenteric mammary gland	- within normal limits - adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b) - hyperplasia, lobular, mild
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1338	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, mild - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1338	E	<b>Microscopic</b> uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - mammary tumor
1339	S	<b>Macroscopic</b> lymph node, axillary  lymph node, inguinal  pituitary gland skin, subcutis	- within normal limits right is draining node for mass b. - not identified, left, no grade draining node for mass a. - enlarged, red, severe - mass, tan, mass a, left anogenital region, present corresponds to antemortem observation (mass 1) approximately 8.0 x 5.0 x 2.3 cm. - mass, tan, mass b, right axillary area, present corresponds to antemortem observation (swelling mass 2) approximately 2.0 x 2.0 x 0.8 cm. - cyst, clear, horn, mild
1339	S	uterus with cervix <b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1339	S	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain  esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, pars distalis, malignant, secondary - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1339	S	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries	- within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - within normal limits - within normal limits - within normal limits - within normal limits - fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b) - hyperplasia, lobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1339	S	<b>Microscopic</b> oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, pars distalis, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1339	S	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix  vagina	- hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild corresponds to macroscopic observation (uterus with cervix - cyst) - within normal limits
1340	E	<b>Macroscopic</b> lymph node, inguinal	- within normal limits draining node for mass a, right.

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1340	E	<b>Macroscopic</b> mammary gland  pituitary gland skin, subcutis	- swollen/thickened, tan, generalized, moderate corresponds to antemortem observation (swelling) - enlarged, red, moderate - mass, tan, mass a, right anogenital region, present corresponds to antemortem observation (swelling mass 1) approximately 3.0 cm in diameter.
1340	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1340	E	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, inguinal lymph node, mandibular lymph node, mesenteric	- within normal limits - hyperplasia, focal, unilateral, minimal - within normal limits - within normal limits - edema, papilla, unilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, eosinophilic, mild - hyperplasia, bile duct, minimal - vacuolation, periportal, mild - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1340	E	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, moderate corresponds to macroscopic observation (mammary gland - swollen/thickened)
		nerve, sciatic	- degeneration, axonal/myelin, minimal
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- cyst, unilateral, minimal
		oviducts	- within normal limits
		pancreas	- atrophy, acinar, minimal
		parathyroid glands	- hyperplasia, focal, bilateral, minimal
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1340	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  thymus thyroid gland tongue trachea ureters	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - hyperplasia, epithelial, nonglandular, moderate - inflammation, mild - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1340	E	<b>Microscopic</b> urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - pituitary tumor
1341	E	<b>Macroscopic</b> lymph node, axillary  pituitary gland skin, subcutis	- within normal limits draining node for mass a, right. - enlarged, mild - mass, tan, mass a, right lateral thorax, present corresponds to antemortem observation (mass 1 scabbed area) approximately 3.0 cm in diameter. ulcerated.
1341	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum	- within normal limits - within normal limits - hyperplasia, mixed, mild - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1341	E	<b>Microscopic</b> bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, unilateral, minimal - mineralization, tubular, unilateral, minimal  - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1341	E	<b>Microscopic</b> lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular	- within normal limits - within normal limits - within normal limits - within normal limits - adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - hyperplasia, diffuse, pars distalis, mild corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1341	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, mild - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits one of pair present

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1341	E	<b>Microscopic</b> urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - mammary tumor
1342	E	<b>Macroscopic</b> lymph node, axillary  skin, subcutis	- within normal limits draining node for mass a, right. - mass, tan, mass a, right axillary area, present corresponds to antemortem observation (mass 1) approximately 10.0 x 10.0 x 7.0 cm.
1342	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1342	E	<b>Microscopic</b> bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1342	E	<b>Microscopic</b> lung lymph node, axillary  lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland	- within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal - histiocytosis, sinus, mild - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1342	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1342	E	<b>Microscopic</b> ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - mammary tumor
1343	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1343	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), severe
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1343	E	<b>Microscopic</b>	
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		gall	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
		kidneys	- mineralization, tubular, unilateral, minimal
		lacrimal glands, exorbital	- within normal limits
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- within normal limits
		liver	- hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal
		lung	- within normal limits
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1343	E	<b>Microscopic</b> mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris	- hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1343	E	<b>Microscopic</b> skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - inflammation, subacute/chronic, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1344	E	<b>Macroscopic</b> animal/whole body  lymph node, axillary  skin, subcutis	- body fat depleted, mild corresponds to antemortem observation (thin) - within normal limits draining node for mass a, right. - mass, tan, mass a, right lateral thorax, present corresponds to antemortem observation (mass 1) approximately 9.0 cm in diameter. wraps around to right axillary area.
1344	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1344	E	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric	 - within normal limits - within normal limits - within normal limits - not examined - within normal limits - within normal limits - within normal limits - mineralization, tubular, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - necrosis, hepatocytes, centrilobular, minimal - vacuolation, centrilobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1344	E	<b>Microscopic</b> mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin	- hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1344	E	<b>Microscopic</b> skin, subcutis	- fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		thymus	- not examined
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		uterus with cervix	- within normal limits
		vagina	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1344	E	<b>Microscopic</b> Cause of Death	- fibrosarcoma/fibroma
1345	E	<b>Macroscopic</b> lymph node, axillary  lymph node, inguinal  mammary gland ovaries pituitary gland skin, subcutis	- within normal limits draining node for mass b, right. - within normal limits draining node for mass a, left. - swollen/thickened, generalized, mild - cyst, clear, right, mild - enlarged, red, severe - mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (swelling) approximately 2.0 x 2.0 x 1.0 cm. - mass, tan, mass b, right axillary area, present corresponds to antemortem observation (swelling) approximately 2.0 x 1.0 x 0.5 cm.
1345	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1345	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain  esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, pars distalis, malignant, secondary - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1345	E	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, inguinal lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic	- within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - vacuolation, periportal, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass b) - hyperplasia, lobular, moderate corresponds to macroscopic observation (mammary gland - swollen/thickened) - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1345	E	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d ovaries  oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - within normal limits - within normal limits - cyst, unilateral, minimal corresponds to macroscopic observation (ovaries - cyst) - within normal limits - within normal limits - not examined - within normal limits - carcinoma, pars distalis, malignant, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1345	E	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - erosion/ulcer, minimal - inflammation, minimal - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1345	E	<b>Microscopic</b> Cause of Death	- pituitary tumor
1346	E	<b>Macroscopic</b> lymph node, axillary  pituitary gland skin, subcutis	- not identified, left, no grade draining node for mass a. - enlarged, red, mild - mass, tan, mass a, left axillary area, present corresponds to antemortem observation (mass 1) approximately 12.5 x 6.5 x 5.0 cm.
1346	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - vacuolation, focal, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1346	E	<b>Microscopic</b> bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - vacuolation, periportal, minimal - histiocytosis, alveolar, minimal

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1346	E	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular	- within normal limits - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1346	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1346	E	<b>Microscopic</b> uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - mammary tumor
1347	S	<b>Macroscopic</b> lymph node, mesenteric	- enlarged, moderate
1347	S	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - within normal limits - hyperplasia, granulocytic, mild - hyperplasia, granulocytic, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1347	S	<b>Microscopic</b> eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - within normal limits - polyarteritis, minimal - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, mild - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - vacuolation, median cleft, mild - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1347	S	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric  mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas  parathyroid glands pharynx	- within normal limits - dilatation, sinus, moderate corresponds to macroscopic observation (lymph node, mesenteric - enlarged) - adenocarcinoma, malignant, primary, incidental, not cause of death slide 18. - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - exudate, nasal passage, minimal - within normal limits - within normal limits - hyperplasia, sex-cord/stromal, unilateral, minimal - within normal limits - atrophy, acinar, minimal - polyarteritis, moderate - not examined - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1347	S	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		thymus	- depletion, lymphoid, generalized, moderate
			- hyperplasia, epithelial cell, minimal
		thyroid gland	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1347	S	<b>Microscopic</b> tongue trachea ureters urinary bladder uterus with cervix vagina	- within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, squamous cell, mild - within normal limits
1348	D	<b>Macroscopic</b> adrenal glands cavity, thoracic  lymph node, mediastinal  pituitary gland thymus	- enlarged, left, mild - mass, tan, mass a, present approximately 4.0 cm in diameter. - within normal limits draining node for mass a. - enlarged, red, mild - not identified, no grade thymus most likely within mass a.

S - Scheduled necropsy  
D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1348	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, unilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged)
		aorta	- within normal limits
		bone marrow, femur	- hyperplasia, granulocytic, mild
		bone marrow, sternum	- hyperplasia, granulocytic, mild
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- not examined autolysis too severe for diagnosis
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, minimal
		joint, tibiofemoral	- within normal limits
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1348	D	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mediastinal lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries	- mineralization, pelvic, bilateral, minimal - pyelitis, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - FEMALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1348	D	<b>Microscopic</b> oviducts pancreas parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- within normal limits - within normal limits - within normal limits one of pair present - within normal limits - hyperplasia, diffuse, pars distalis, mild corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1348	D	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - thymoma, malignant, primary, fatal, positive cause of death corresponds to macroscopic observation (cavity, thoracic - mass a) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - thymus tumor
1349	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass a, left.

E - Euthanized *in extremis*

D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1349	E	<b>Macroscopic</b> pituitary gland skin, subcutis	- enlarged, red, severe - mass, tan, mass a, left axillary area, present corresponds to antemortem observation (swelling) approximately 1.0 x 1.0 x 0.5 cm.
1349	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1349	E	<b>Microscopic</b> heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland	- cardiomyopathy, minimal - within normal limits - hyperplasia, transitional cell, bilateral, minimal - pyelitis, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, eosinophilic, minimal - vacuolation, periportal, minimal - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, moderate

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1349	E	<b>Microscopic</b> nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1349	E	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1350	D	<b>Macroscopic</b> all tissues	- within normal limits
1350	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1350	D	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung  lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c	- mineralization, pelvic, bilateral, minimal - mineralization, tubular, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - bacterial colonies, minimal large amount of section has lysed red blood cells indicative of dosing injury. - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1350	D	<b>Microscopic</b> nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1350	D	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dosing injury
1351	D	<b>Macroscopic</b> eyes  eyes, optic nerves	- absent/cannibalized, bilateral, no grade corresponds to antemortem observation (cannibalized/partially cannibalized) - absent/cannibalized, bilateral, no grade
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1351	D	<b>Macroscopic</b> eyes, retina harderian glands lacrimal glands, exorbital lymph node, axillary  lymph node, mandibular parathyroid glands pituitary gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skin, subcutis  thyroid gland	<ul style="list-style-type: none"> <li>- absent/cannibalized, bilateral, no grade</li> <li>- absent/cannibalized, bilateral, no grade</li> <li>- absent/cannibalized, bilateral, no grade</li> <li>- within normal limits</li> <li>draining node for mass a, left. draining node for mass b, right.</li> <li>- absent/cannibalized, bilateral, no grade</li> <li>- absent/cannibalized, bilateral, no grade</li> <li>- enlarged, red, severe</li> <li>- absent/cannibalized, bilateral, no grade</li> <li>- absent/cannibalized, bilateral, no grade</li> <li>- absent/cannibalized, bilateral, no grade</li> <li>- mass, tan, mass b, right axillary area, present</li> <li>corresponds to antemortem observation (mass 2)</li> <li>approximately 4.0 cm in diameter.</li> <li>- mass, ulcerated, mass a, left axillary area, present</li> <li>corresponds to antemortem observation (mass 1 hair sparse)</li> <li>approximately 9.0 x 6.0 x 5.0 cm, tan.</li> <li>- absent/cannibalized, bilateral, no grade</li> </ul>

D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1351	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), mild
		esophagus	- within normal limits
		eyes	- not examined cannibalized
		eyes, optic nerves	- not examined cannibalized
		eyes, retina	- not examined cannibalized
		galt	- within normal limits
		harderian glands	- not examined cannibalized
		heart	- cardiomyopathy, minimal
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1351	D	<b>Microscopic</b> joint, tibiofemoral kidneys  lacrimal glands, exorbital  large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, mandibular  lymph node, mesenteric	- within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, bilateral, minimal - not examined cannibalized - within normal limits - within normal limits - within normal limits - not examined - within normal limits - within normal limits - within normal limits - not examined cannibalized - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1351	D	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b) - hyperplasia, lobular, mild
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- not examined cannibalized
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- not examined cannibalized
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1351	D	<b>Microscopic</b> salivary gland, parotid	- not examined cannibalized
		salivary gland, sublingual	- not examined cannibalized
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		thymus	- depletion, lymphoid, generalized, severe
		thyroid gland	- not examined cannibalized
		tongue	- within normal limits
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1351	D	<b>Microscopic</b> trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1352	S	<b>Macroscopic</b> lymph node, inguinal  lymph node, mandibular  mammary gland  ovaries	- not identified, bilateral, no grade draining node for mass b, left. draining node for mass c, right. - within normal limits draining node for mass a, right. - swollen/thickened, tan, moderate most affected areas are left inguinal region, right inguinal region and anogenital region. - cyst, clear, left, mild
S - Scheduled necropsy D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1352	S	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, cervical, present corresponds to antemortem observation (mass 1) approximately 2.0 x 4.5 x 5.0 cm.</li> <li>- mass, tan, mass b, left anogenital region, present corresponds to antemortem observation (nodule) approximately 1.0 x 1.5 x 2.0 cm.</li> <li>- mass, tan, mass c, right inguinal area, present corresponds to antemortem observation (nodule) approximately 0.5 x 1.5 x 2.0 cm.</li> </ul>
1352	S	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum	<ul style="list-style-type: none"> <li>- angiectasis/cystic degeneration, focal cortical, bilateral, moderate</li> <li>- hyperplasia, focal medullary, unilateral, minimal</li> <li>- within normal limits</li> <li>- hyperplasia, granulocytic, mild</li> <li>- hyperplasia, granulocytic, minimal</li> <li>- within normal limits</li> <li>- within normal limits</li> </ul>
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1352	S	<b>Microscopic</b> brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands  heart  joint, tibiofemoral kidneys  lacrimal glands, exorbital  large intestine, cecum large intestine, colon large intestine, rectum	- lymphoma, malignant, multicentric, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - lymphoma, malignant, multicentric, incidental, not cause of death - lymphoma, malignant, bilateral, multicentric, incidental, not cause of death - cardiomyopathy, mild - lymphoma, malignant, multicentric, incidental, not cause of death - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - lymphoma, malignant, bilateral, multicentric, incidental, not cause of death - polyarteritis, minimal - lymphoma, malignant, multicentric, incidental, not cause of death - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1352	S	<b>Microscopic</b> larynx liver  lung  lymph node, inguinal  lymph node, mandibular  lymph node, mesenteric	- lymphoma, malignant, multicentric, incidental, not cause of death - focus of cellular alteration, basophilic, minimal - lymphoma, malignant, multicentric, incidental, not cause of death - necrosis, focal, minimal - vacuolation, centrilobular, minimal - histiocytosis, alveolar, minimal - lymphoma, malignant, multicentric, incidental, not cause of death - lymphoma, malignant, multicentric, incidental, not cause of death slide 26-3 and 26-3 r-1. - hyperplasia, lymphocyte/plasmacyte, medulla, mild - lymphoma, malignant, multicentric, incidental, not cause of death - lymphoma, malignant, multicentric, incidental, not cause of death
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1352	S	<b>Microscopic</b> mammary gland	<ul style="list-style-type: none"> <li>- adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass b)</li> <li>- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass c)</li> <li>- hyperplasia, lobular, moderate corresponds to macroscopic observation (mammary gland - swollen/thickened)</li> </ul>
		multicentric neoplasm	- lymphoma, malignant, multicentric, incidental, not cause of death
		nerve, sciatic	- degeneration, axonal/myelin, minimal
		nose, level a	- lymphoma, malignant, multicentric, incidental, not cause of death
		nose, level b	- lymphoma, malignant, multicentric, incidental, not cause of death
		nose, level c	- lymphoma, malignant, multicentric, incidental, not cause of death
		nose, level d	- lymphoma, malignant, multicentric, incidental, not cause of death
		ovaries	<ul style="list-style-type: none"> <li>- cyst, unilateral, mild corresponds to macroscopic observation (ovaries - cyst)</li> <li>- hyperplasia, sex-cord/stromal, unilateral, minimal</li> </ul>
		oviducts	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1352	S	<b>Microscopic</b> pancreas  parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar	- hyperplasia, islet cell, mild - lymphoma, malignant, multicentric, incidental, not cause of death - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - lymphoma, malignant, multicentric, incidental, not cause of death - lymphoma, malignant, multicentric, incidental, not cause of death - lymphoma, malignant, multicentric, incidental, not cause of death - within normal limits - lymphoma, malignant, multicentric, incidental, not cause of death slide 8, 18, 18-1, 26-1, 26-2, 26-3, and 26-3 r-1. - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1352	S	<b>Microscopic</b> spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland  tongue trachea ureters  urinary bladder uterus with cervix  vagina	- within normal limits - lymphoma, malignant, multicentric, incidental, not cause of death - within normal limits - lymphoma, malignant, multicentric, incidental, not cause of death - depletion, lymphoid, generalized, severe - hyperplasia, epithelial cell, mild - lymphoma, malignant, bilateral, multicentric, incidental, not cause of death - within normal limits - within normal limits - lymphoma, malignant, unilateral, multicentric, incidental, not cause of death - lymphoma, malignant, multicentric, incidental, not cause of death - dilatation, gland/lumen, mild - lymphoma, malignant, multicentric, incidental, not cause of death - within normal limits
1353	S	<b>Macroscopic</b> adrenal glands	- enlarged, tan, right, mild
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1353	S	<b>Macroscopic</b> lymph node, axillary  lymph node, iliac  lymph node, inguinal  pituitary gland skin, subcutis	<ul style="list-style-type: none"> <li>- within normal limits draining node for mass d, left.</li> <li>- within normal limits draining node for mass c, right.</li> <li>- not identified, right, no grade draining node for mass a and mass b.</li> <li>- enlarged, tan, mild</li> <li>- mass, black, mass c, right anogenital region, present approximately 5.5 x 3.5 x 2.0 cm.</li> <li>- mass, tan, mass a, right inguinal area, present corresponds to antemortem observation (mass 1) approximately 6.0 x 4.0 x 3.5 cm.</li> <li>- mass, tan, mass b, right inguinal area, present corresponds to antemortem observation (mass 2) approximately 2.5 x 2.5 x 2.0 cm.</li> <li>- mass, tan, mass d, left axillary area, present corresponds to antemortem observation (swelling) approximately 2.5 x 1.5 x 1.5 cm.</li> </ul>
S - Scheduled necropsy			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1353	S	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged) one medulla present
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, minimal
		joint, tibiofemoral	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1353	S	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, iliac lymph node, mandibular lymph node, mesenteric	- mineralization, pelvic, bilateral, mild - mineralization, tubular, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, eosinophilic, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1353	S	<b>Microscopic</b> mammary gland	- adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass b; skin, subcutis - mass c; skin, subcutis - mass d) - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- cyst, unilateral, minimal
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1353	S	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- degeneration/necrosis, myofiber, minimal
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1353	S	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, moderate
			- hyperplasia, epithelial cell, mild
		thyroid gland	- hyperplasia, c-cell, focal, unilateral, mild
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		uterus with cervix	- dilatation, gland/lumen, mild
		vagina	- within normal limits
1354	E	<b>Macroscopic</b> pituitary gland	- enlarged, moderate
1354	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild
			- hyperplasia, focal cortical, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1354	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum	 - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, unilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1354	E	<b>Microscopic</b> larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas	- within normal limits - fibrosis, minimal - macrophages, pigmented, minimal - vacuolation, periportal, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - adenocarcinoma, malignant, primary, incidental, not cause of death slide 18. - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - cyst, unilateral, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1354	E	<b>Microscopic</b> parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular	- within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1354	E	<b>Microscopic</b> stomach, nonglandular thymus thyroid gland tongue  trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, c-cell, focal, unilateral, minimal - hyperplasia, squamous cell, moderate - inflammation, subacute/chronic, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1355	S	<b>Macroscopic</b> adrenal glands pituitary gland	- small, right, mild - enlarged, red, severe
1355	S	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - hyperplasia, focal medullary, unilateral, minimal

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1355	S	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1355	S	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas	- within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, eosinophilic, moderate - hyperplasia, bile duct, mild - vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1355	S	<b>Microscopic</b> parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular	- within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1355	S	<b>Microscopic</b> stomach, nonglandular thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina non-correlated macro observation	- within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, bilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adrenal glands - small
1356	E	<b>Macroscopic</b> adrenal glands liver lymph node, axillary	- enlarged, bilateral, mild - focus/foci, red, multiple lobes, mild - within normal limits draining node for mass a, left and mass g, right.
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - FEMALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1356	E	<b>Macroscopic</b> lymph node, inguinal  lymph node, mandibular  pituitary gland	- not identified, bilateral, no grade draining node for mass b and mass e, left and mass c, right. - within normal limits draining lymph node for mass d, left and mass f, right. - enlarged, red, severe
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1356	E	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, left axillary area, present corresponds to antemortem observation (mass 1) approximately 3.0 x 2.5 x 1.5 cm.</li> <li>- mass, tan, mass b, left inguinal area, present corresponds to antemortem observation (mass 2) approximately 2.5 x 1.5 x 1.0 cm.</li> <li>- mass, tan, mass c, right inguinal area, present corresponds to antemortem observation (swelling) approximately 3.5 x 2.5 x 1.5 cm.</li> <li>- mass, tan, mass d, left lateral neck, present approximately 2.5 x 1.0 x 0.75 cm.</li> <li>- mass, tan, mass e, left anogenital region, present approximately 2.0 x 1.75 x 1.0 cm.</li> <li>- mass, tan, mass f, right lateral neck, present approximately 3.0 x 1.5 x 1.0 cm.</li> <li>- mass, tan, mass g, right axillary area, present corresponds to antemortem observation (swelling) approximately 2.0 x 1.0 x 0.5 cm.</li> </ul>
		tongue	<ul style="list-style-type: none"> <li>- focus/foci, tan, mild</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1356	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged)
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), moderate
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
		kidneys	- mineralization, pelvic, bilateral, minimal
E - Euthanized <i>in extremis</i>			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1356	E	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - necrosis, focal, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1356	E	<b>Microscopic</b> mammary gland	- adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b; skin, subcutis - mass c; skin, subcutis - mass d; skin, subcutis - mass e; skin, subcutis - mass f; skin, subcutis - mass g)
		nerve, sciatic	- hyperplasia, lobular, mild
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- not examined
		pharynx	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1356	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		thymus	- depletion, lymphoid, generalized, moderate
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1356	E	<b>Microscopic</b> thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina non-correlated macro observation  Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - liver - focus/foci, red - tongue - focus/foci, tan - pituitary tumor
1357	S	<b>Macroscopic</b> lymph node, mandibular  pituitary gland skin, subcutis	- within normal limits draining node for mass a, bilateral. - enlarged, red, mild - mass, tan, mass a, ventral neck, present corresponds to antemortem observation (swelling) approximately 2.5 cm in diameter.
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1357	S	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - hyperplasia, focal medullary, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, minimal
		joint, tibiofemoral	- within normal limits
		kidneys	- mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1357	S	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - within normal limits - within normal limits - within normal limits - adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1357	S	<b>Microscopic</b> pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen	- within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1357	S	<b>Microscopic</b> stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix  vagina	- within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperkeratosis, mild - hyperplasia, squamous cell, mild - within normal limits
1358	S	<b>Macroscopic</b> lung with bronchi lymph node, axillary	- focus/foci, tan, left lobe, mild - within normal limits draining node for mass b, left.
S - Scheduled necropsy			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1358	S	<b>Macroscopic</b> lymph node, mandibular  pituitary gland skin, subcutis	- within normal limits draining node for mass a, left. - enlarged, mild - mass, tan, mass a, ventral neck, present corresponds to antemortem observation (mass 1) approximately 4.0 cm in diameter. - mass, tan, mass b, left axillary area, present corresponds to antemortem observation (swelling) approximately 1.5 cm in diameter.
1358	S	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1358	S	<b>Microscopic</b> esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - dilatation, tubular, unilateral, minimal - hydronephrosis, unilateral, mild - mineralization, pelvic, bilateral, mild - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1358	S	<b>Microscopic</b> liver	- focus of cellular alteration, basophilic, minimal
		lung	- hyperplasia, bile duct, minimal - histiocytosis, alveolar, mild corresponds to macroscopic observation (lung with bronchi - focus/foci, tan)
		lymph node, axillary	- within normal limits
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
		mammary gland	- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b)
		nerve, sciatic	- hyperplasia, lobular, mild
		nose, level a	- degeneration, axonal/myelin, minimal
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1358	S	<b>Microscopic</b> pancreas parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- within normal limits - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1358	S	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix  vagina	- hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - hyperplasia, c-cell, focal, unilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild - hyperkeratosis, minimal - hyperplasia, squamous cell, mild - within normal limits
1359	E	<b>Macroscopic</b> animal/whole body  pituitary gland	- body fat depleted, moderate corresponds to antemortem observation (thin) - enlarged, red, severe

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1359	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), severe
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
		kidneys	- mineralization, pelvic, bilateral, minimal
			- mineralization, tubular, unilateral, minimal
		lacrimal glands, exorbital	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1359	E	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands	- within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, mild - within normal limits one of pair present

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1359	E	<b>Microscopic</b> pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular	- within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1359	E	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- depletion, lymphoid, generalized, severe - hyperplasia, c-cell, focal, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1360	D	<b>Macroscopic</b> lymph node, inguinal  pituitary gland skin, subcutis  uterus with cervix	- not identified, left, no grade draining node for mass a. - enlarged, severe - mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 4.0 cm in diameter. - enlarged, horn, mild
E - Euthanized <i>in extremis</i> D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1360	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain  esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, pars distalis, malignant, secondary - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1360	D	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a  nose, level b  nose, level c	- within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - multinucleated, hepatocytes, minimal - within normal limits - within normal limits - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - foreign material, mild plant. - foreign material, moderate plant. - foreign material, moderate plant.
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1360	D	<b>Microscopic</b> nose, level d  ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum	- foreign material, minimal plant. - hyperplasia, sex-cord/stromal, unilateral, minimal - within normal limits - within normal limits - not examined - within normal limits - carcinoma, pars distalis, malignant, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1360	D	<b>Microscopic</b> spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular  stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix  vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - erosion/ulcer, mild - inflammation, mild - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild corresponds to macroscopic observation (uterus with cervix - enlarged) - within normal limits - pituitary tumor
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1361	D	<b>Macroscopic</b> lymph node, axillary  lymph node, inguinal  pituitary gland skin, subcutis	- within normal limits draining node for mass b, left. - not identified, left, no grade draining node for mass a. may be encompassed in mass a. - enlarged, severe - mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 8.0 x 6.0 x 4.0 cm. - mass, tan, mass b, left axillary area, present approximately 2.5 x 2.0 x 0.5 cm.
1361	D	<b>Microscopic</b> adrenal glands   aorta bone marrow, femur bone marrow, sternum	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - ganglioneuroma, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1361	D	<b>Microscopic</b> bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	 - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, unilateral, minimal  - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1361	D	<b>Microscopic</b> liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas	- focus of cellular alteration, basophilic, minimal - vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - within normal limits - fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b) - hyperplasia, lobular, minimal - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - cyst, unilateral, minimal - within normal limits - within normal limits
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1361	D	<b>Microscopic</b> parathyroid glands	- within normal limits one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		skin, subcutis	- fibroma, benign, primary, incidental, not cause of death slide 18.
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1361	D	<b>Microscopic</b> spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - hematopoiesis, extramedullary, increased, mild - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1362	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass b and mass f, right.

E - Euthanized *in extremis*

D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - FEMALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1362	E	<b>Macroscopic</b> lymph node, inguinal	- not identified, bilateral, no grade draining node for mass a and mass c, left. draining node for mass d and mass e, right.
		lymph node, mandibular	- within normal limits draining node for mass g, right.
		pituitary gland	- enlarged, moderate
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1362	E	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, left anogenital region, present corresponds to antemortem observation (skin discolored mass 1) approximately 7.0 cm in diameter.</li> <li>- mass, tan, mass b, right axillary area, present corresponds to antemortem observation (mass 2 swelling) approximately 1.2 cm in diameter.</li> <li>- mass, tan, mass c, left inguinal area, present approximately 2.2 cm in diameter.</li> <li>- mass, tan, mass d, right inguinal area, present approximately 1.2 cm in diameter.</li> <li>- mass, tan, mass e, right inguinal area, present approximately 1.9 cm in diameter.</li> <li>- mass, tan, mass f, right axillary area, present corresponds to antemortem observation (swelling) approximately 1.8 cm in diameter.</li> <li>- mass, tan, mass g, right lateral neck, present approximately 1.0 cm in diameter.</li> </ul>
1362	E	<b>Microscopic</b> adrenal glands	<ul style="list-style-type: none"> <li>- vacuolation, focal, unilateral, minimal</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1362	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, bilateral, mild - pyelitis, unilateral, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1362	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1362	E	<b>Microscopic</b> mammary gland	<ul style="list-style-type: none"> <li>- adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass b; skin, subcutis - mass d; skin, subcutis - mass f) mass d has both an adenocarcinoma and a fibroadenoma.</li> <li>- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass c; skin, subcutis - mass d; skin, subcutis - mass e; skin, subcutis - mass g)</li> <li>- hyperplasia, lobular, minimal</li> </ul>
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1362	E	<b>Microscopic</b> parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen	- within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1362	E	<b>Microscopic</b> stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, minimal - within normal limits - mammary tumor
1363	D	<b>Macroscopic</b> liver lymph node, inguinal	- focus/foci, tan, left lateral lobe, mild - not identified, left, no grade draining node for mass a.
E - Euthanized <i>in extremis</i> D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1363	D	<b>Macroscopic</b> skin, subcutis	- mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 12.5 x 10.0 x 5.0 cm.
1363	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - hyperplasia, granulocytic, mild - hyperplasia, granulocytic, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1363	D	<b>Microscopic</b> joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic	- within normal limits - mineralization, pelvic, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - necrosis, focal, moderate corresponds to macroscopic observation (liver - focus/foci, tan) - within normal limits - within normal limits - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, minimal - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1363	D	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1363	D	<b>Microscopic</b> spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mammary tumor
1364	E	<b>Macroscopic</b> lymph node, inguinal	- within normal limits draining node for mass a, left.

E - Euthanized *in extremis*  
D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1364	E	<b>Macroscopic</b> pituitary gland skin, subcutis	- enlarged, red, severe - mass, ulcerated, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 7.0 x 5.0 x 3.0 cm, tan.
1364	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - hyperplasia, granulocytic, mild - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1364	E	<b>Microscopic</b> heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, inguinal  lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - hydronephrosis, unilateral, moderate - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - hematopoiesis, extramedullary, minimal - vacuolation, periportal, minimal - within normal limits - not examined misidentified tissue - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1364	E	<b>Microscopic</b> mammary gland	- adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1364	E	<b>Microscopic</b> salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, mild - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - dilatation, unilateral, mild - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1364	E	<b>Microscopic</b> vagina Cause of Death	- within normal limits - mammary tumor
1365	S	<b>Macroscopic</b> pituitary gland	- enlarged, tan, moderate
1365	S	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - hyperplasia, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1365	S	<b>Microscopic</b> eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrima glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - dilatation, tubular, unilateral, minimal - edema, papilla, unilateral, mild - hydronephrosis, unilateral, mild - nephropathy, chronic progressive, bilateral, mild - within normal limits - erosion/ulcer, mild - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - histiocytosis, alveolar, minimal
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1365	S	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid	- within normal limits - within normal limits - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1365	S	<b>Microscopic</b> salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix	- within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1365	S	<b>Microscopic</b> vagina	- within normal limits
1366	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass a, right.
		lymph node, brachial	- within normal limits draining node for mass a, right.
		lymph node, inguinal	- not identified, right, no grade draining node for mass b.
		pituitary gland	- enlarged, red, moderate
		skin, subcutis	- mass, tan, mass a, right axillary area, present corresponds to antemortem observation (mass 1) approximately 10.0 x 8.0 x 3.0 cm.
			- mass, tan, mass b, right inguinal area, present corresponds to antemortem observation (skin discolored mass 2) approximately 6.0 x 5.2 x 2.2 cm.
1366	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate

S - Scheduled necropsy  
E - Euthanized *in extremis*

## Terminal

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1366	E	<b>Microscopic</b> larynx liver lung lymph node, axillary lymph node, brachial lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts	- within normal limits - focus of cellular alteration, basophilic, minimal - histiocytosis, alveolar, minimal - within normal limits - not examined - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass b) - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, minimal - within normal limits - within normal limits - exudate, nasal passage, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1366	E	<b>Microscopic</b> pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen	- within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1366	E	<b>Microscopic</b> stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild - within normal limits - mammary tumor
1367	E	<b>Macroscopic</b> lymph node, inguinal  skin, subcutis	- absent, left, no grade draining node for mass a. - mass, tan, mass a, anogenital region, present corresponds to antemortem observation (mass 1) approximately 7.0 x 6.0 x 4.0 cm.
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1367	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1367	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas	- within normal limits - within normal limits - within normal limits - focus of cellular alteration, eosinophilic, minimal - hyperplasia, bile duct, mild - within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - dilatation, gland/lumen, mild - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1367	E	<b>Microscopic</b> parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular	- hyperplasia, focal, unilateral, minimal one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1367	E	<b>Microscopic</b> thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, endometrial, mild - within normal limits - mammary tumor
1368	S	<b>Macroscopic</b> lymph node, inguinal  skin, subcutis	- not identified, right, no grade draining node for mass a. - mass, tan, mass a, right inguinal area, present corresponds to antemortem observation (mass 1) approximately 8.0 cm in diameter.

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1368	S	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1368	S	<b>Microscopic</b> kidneys	<ul style="list-style-type: none"> <li>- edema, papilla, bilateral, mild</li> <li>- hydronephrosis, bilateral, mild</li> <li>- hyperplasia, transitional cell, bilateral, minimal</li> <li>- macrophages, pigmented, unilateral, minimal</li> <li>- mineralization, tubular, bilateral, minimal</li> </ul>
		lacrimal glands, exorbital	- within normal limits
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- within normal limits
		liver	<ul style="list-style-type: none"> <li>- angiectasis, minimal</li> <li>- focus of cellular alteration, basophilic, mild</li> <li>- focus of cellular alteration, eosinophilic, minimal</li> <li>- hyperplasia, bile duct, minimal</li> </ul>
		lung	- within normal limits
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
S - Scheduled necropsy			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1368	S	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) slide 18 and 26-1.
		nerve, sciatic	- hyperplasia, lobular, mild
		nose, level a	- degeneration, axonal/myelin, minimal
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- hyperplasia, focal, unilateral, mild one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1368	S	<b>Microscopic</b> salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder	- within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, mild - within normal limits - within normal limits - within normal limits - dilatation, bilateral, mild - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1368	S	<b>Microscopic</b> uterus with cervix	- dilatation, gland/lumen, mild - hyperplasia, endometrial, mild
		vagina	- within normal limits
1369	E	<b>Macroscopic</b> cavity, thoracic	- fluid, red, minimal approximately 1.0 ml of fluid.
		mammary gland	- swollen/thickened, tan, inguinal, left, mild corresponds to antemortem observation (swelling)
		pituitary gland	- enlarged, tan, moderate
		skin	- abrasion/scab, inguinal, right, moderate corresponds to antemortem observation (mass 1)
		spleen	- enlarged, mild
1369	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - hyperplasia, focal cortical, unilateral, mild
		aorta	- within normal limits

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1369	E	<b>Microscopic</b> bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum	 - hyperplasia, granulocytic, mild - hyperplasia, granulocytic, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1369	E	<b>Microscopic</b> larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx	- within normal limits - focus of cellular alteration, basophilic, minimal - hematopoiesis, extramedullary, minimal - within normal limits - within normal limits - within normal limits - hyperplasia, lobular, mild corresponds to macroscopic observation (mammary gland - swollen/thickened) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, sex-cord/stromal, bilateral, mild - within normal limits - within normal limits - not examined - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1369	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- erosion/ulcer, moderate corresponds to macroscopic observation (skin - abrasion/scab)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, mild corresponds to macroscopic observation (spleen - enlarged)
		stomach, glandular	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1369	E	<b>Microscopic</b> stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - skin inflammation/necrosis
1370	S	<b>Macroscopic</b> pituitary gland	- cyst, clear, mild
1370	S	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1370	S	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1370	S	<b>Microscopic</b> large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx	- within normal limits - within normal limits - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - hyperplasia, lobular, minimal - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1370	S	<b>Microscopic</b> pituitary gland	- cyst, moderate corresponds to macroscopic observation (pituitary gland - cyst)
		salivary gland, mandibular	- hyperplasia, focal, pars distalis, mild
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- degeneration/necrosis, myofiber, minimal
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		thymus	- depletion, lymphoid, generalized, moderate
		thyroid gland	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1370	S	<b>Microscopic</b> tongue trachea ureters urinary bladder uterus with cervix vagina	- within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild - within normal limits
1371	E	<b>Macroscopic</b> all tissues	- within normal limits
1371	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1371	E	<b>Microscopic</b> esophagus eyes eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, tubular, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1371	E	<b>Microscopic</b> nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas  parathyroid glands  pharynx pituitary gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1371	E	<b>Microscopic</b> small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - carcinoma, follicular cell, malignant, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1372	S	<b>Macroscopic</b> lymph node, mandibular  skin, subcutis	- within normal limits bilateral, draining node for mass a. - mass, tan, mass a, ventral neck, present corresponds to antemortem observation (mass 1) approximately 7.0 x 5.5 x 2.0 cm.
1372	S	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1372	S	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys  lacrimial glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland	- within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - mineralization, tubular, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - within normal limits - within normal limits - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild
S - Scheduled necropsy			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1372	S	<b>Microscopic</b> nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1372	S	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina	- within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
1373	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass b, right.

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1373	E	<b>Macroscopic</b> lymph node, inguinal  pituitary gland skin, subcutis	- within normal limits draining node for mass a, left. - enlarged, red, mild - mass, tan, mass a, anogenital region, present corresponds to antemortem observation (mass 1) approximately 3.0 x 1.5 x 1.0 cm. - mass, ulcerated, mass b, right axillary area, present corresponds to antemortem observation (scabbed area mass 2) approximately 6.0 cm in diameter, tan.
1373	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus	- angiectasis/cystic degeneration, focal cortical, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), minimal - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1373	E	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, inguinal lymph node, mandibular lymph node, mesenteric	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1373	E	<b>Microscopic</b> mammary gland	<ul style="list-style-type: none"> <li>- adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)</li> <li>- adenoma, benign, primary, incidental, not cause of death slide 18.</li> <li>- fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass b)</li> <li>- hyperplasia, lobular, mild</li> <li>- degeneration, axonal/myelin, minimal</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- atrophy, acinar, minimal</li> <li>- not examined</li> <li>- within normal limits</li> </ul>
		nerve, sciatic	
		nose, level a	
		nose, level b	
		nose, level c	
		nose, level d	
		ovaries	
		oviducts	
		pancreas	
		parathyroid glands	
		pharynx	

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1373	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1373	E	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, severe
			- hyperplasia, epithelial cell, minimal
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		uterus with cervix	- metaplasia, squamous, minimal
		vagina	- within normal limits
		Cause of Death	- mammary tumor
1374	S	<b>Macroscopic</b> adrenal glands	- enlarged, right, mild
		lymph node, inguinal	- within normal limits
			draining node for mass a, left. draining node for mass b, right.

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1374	S	<b>Macroscopic</b> skin, subcutis	- mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 6.0 x 3.0 x 1.0 cm. - mass, tan, mass b, right inguinal area, present approximately 1.0 cm in diameter. - enlarged, horn, mild
1374	S	uterus with cervix <b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1374	S	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, inguinal	 - within normal limits - within normal limits - degeneration/atrophy, retina, bilateral, mild - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - vacuolation, focal, minimal - histiocytosis, alveolar, minimal - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1374	S	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric mammary gland   nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx	- within normal limits - within normal limits - adenocarcinoma, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (skin, subcutis - mass b) - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1374	S	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- degeneration/necrosis, myofiber, minimal
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- cyst, keratin, minimal
		thymus	- depletion, lymphoid, generalized, moderate
			- hyperplasia, epithelial cell, minimal
		thyroid gland	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1374	S	<b>Microscopic</b> tongue trachea ureters urinary bladder uterus with cervix	- within normal limits - within normal limits - within normal limits - within normal limits - granular cell tumor, benign, primary, incidental, not cause of death - hyperplasia, cystic endometrial, mild corresponds to macroscopic observation (uterus with cervix - enlarged)
1375	E	vagina <b>Macroscopic</b> liver lymph node, inguinal  mammary gland  pituitary gland	- within normal limits  - cyst, clear, caudate lobe, mild - within normal limits draining node for mass a, left. - swollen/thickened, ventral abdomen, left axillary area, mild corresponds to antemortem observation (swelling) - enlarged, severe

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1375	E	<b>Macroscopic</b> skin, subcutis	- mass, brown, mass a, left anogenital region, present corresponds to antemortem observation (mass 1) approximately 2.0 cm in diameter.
1375	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1375	E	<b>Microscopic</b> heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, inguinal lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - nephropathy, chronic progressive, bilateral, minimal - pyelitis, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cyst, biliary, simple, mild corresponds to macroscopic observation (liver - cyst) - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1375	E	<b>Microscopic</b> mammary gland	- adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild corresponds to macroscopic observation (mammary gland - swollen/thickened)
		nerve, sciatic	- degeneration, axonal/myelin, minimal
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- cyst, unilateral, mild - hyperplasia, sex-cord/stromal, unilateral, minimal
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- not examined
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1375	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits one of pair present

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1375	E	<b>Microscopic</b> urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - pituitary tumor
1376	E	<b>Macroscopic</b> adrenal glands lymph node, axillary  lymph node, inguinal  skin, subcutis   uterus with cervix	- enlarged, red, moderate - within normal limits draining node for mass b, right. - within normal limits draining node for mass a, right. - mass, tan, mass b, right axillary area, present corresponds to antemortem observation (swelling) approximately 4.5 cm in diameter. - mass, ulcerated, mass a, right inguinal area, present corresponds to antemortem observation (mass 1) approximately 11.0 x 8.0 x 3.0 cm, tan. - enlarged, horn, mild

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1376	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, severe corresponds to macroscopic observation (adrenal glands - enlarged)
		aorta	- atrophy, cortical, unilateral, severe
		bone marrow, femur	- mineralization, mild
		bone marrow, sternum	- hyperplasia, granulocytic, mild
		bone, femur	- hyperplasia, granulocytic, minimal
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, mild
		joint, tibiofemoral	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1376	E	<b>Microscopic</b> kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, inguinal lymph node, mandibular lymph node, mesenteric	- nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, clear, mild - focus of cellular alteration, eosinophilic, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - necrosis, focal, minimal - hemorrhage, minimal - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1376	E	<b>Microscopic</b> mammary gland	- adenocarcinoma, malignant, primary, incidental, not cause of death slide 18 r-1. - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass b) - hyperplasia, lobular, moderate - degeneration, axonal/myelin, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- cyst, bilateral, mild
		oviducts	- within normal limits
		pancreas	- atrophy, acinar, minimal
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		salivary gland, mandibular	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1376	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea	- within normal limits - within normal limits - within normal limits - within normal limits - fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, mild - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1376	E	<b>Microscopic</b> ureters urinary bladder uterus with cervix	- within normal limits - within normal limits - dilatation, gland/lumen, mild corresponds to macroscopic observation (uterus with cervix - enlarged) - hyperplasia, endometrial, mild - within normal limits
1377	D	Cause of Death <b>Macroscopic</b> eyes  eyes, retina  tongue	- fibrosarcoma/fibroma  - absent/cannibalized, left, no grade corresponds to antemortem observation (cannibalized/partially cannibalized) - absent/cannibalized, left, no grade corresponds to antemortem observation (cannibalized/partially cannibalized) - absent portion/cannibalized, no grade corresponds to antemortem observation (cannibalized/partially cannibalized)
1377	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, unilateral, mild

E - Euthanized *in extremis*

D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1377	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes  eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - not examined one cannibalized, one too autolytic to examine. - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1377	D	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver lung  lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands	- within normal limits - within normal limits - within normal limits - vacuolation, periportal, mild - bacterial colonies, minimal red blood cell lysis in alveolar septae. - within normal limits - within normal limits - hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits one of pair present
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1377	D	<b>Microscopic</b> pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland	- within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1377	D	<b>Microscopic</b> tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - not examined - within normal limits - within normal limits - probable dosing injury
1378	D	<b>Macroscopic</b> pituitary gland	- enlarged, mild
1378	D	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - within normal limits - hyperplasia, granulocytic, mild - hyperplasia, granulocytic, mild - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1378	D	<b>Microscopic</b> bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver	- within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - dilatation, tubular, bilateral, mild - edema, papilla, bilateral, mild - mineralization, pelvic, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1378	D	<b>Microscopic</b> lung lymph node, mandibular lymph node, mesenteric mammary gland mesentery/peritoneum  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries  oviducts pancreas parathyroid glands  pharynx	- within normal limits - within normal limits - within normal limits - hyperplasia, lobular, minimal - polyarteritis, moderate slide 11 and 12. - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cyst, unilateral, mild - hyperplasia, sex-cord/stromal, bilateral, mild - within normal limits - polyarteritis, moderate - within normal limits one of pair present - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1378	D	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		thymus	- depletion, lymphoid, generalized, moderate
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1378	D	<b>Microscopic</b> thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1379	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1379	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1379	E	<b>Microscopic</b> bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung	 - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, pelvic, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1379	E	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx pituitary gland  salivary gland, mandibular	- erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits - hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1379	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, mild - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1379	E	<b>Microscopic</b> urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - pituitary tumor
1380	E	<b>Macroscopic</b> lymph node, inguinal  pituitary gland skin, subcutis	- not identified, left, no grade draining node for mass a. - enlarged, tan, mild - mass, ulcerated, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 8.0 cm in diameter, tan.
1380	E	<b>Microscopic</b> adrenal glands  aorta	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - hematopoiesis, extramedullary, bilateral, minimal - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1380	E	<b>Microscopic</b> bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum	 - hyperplasia, granulocytic, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1380	E	<b>Microscopic</b> larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands	- within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - vacuolation, diffuse, mild - within normal limits - within normal limits - within normal limits - adenocarcinoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1380	E	<b>Microscopic</b> pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular	- within normal limits - hyperplasia, diffuse, pars distalis, mild corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, mild - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1380	E	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, severe - hyperplasia, epithelial cell, minimal
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		uterus with cervix	- within normal limits
		vagina	- within normal limits
		Cause of Death	- mammary tumor
1381	E	<b>Macroscopic</b> pituitary gland	- enlarged, severe
1381	E	<b>Microscopic</b> adrenal glands	- within normal limits
		aorta	- within normal limits
		bone marrow, femur	- within normal limits

E - Euthanized *in extremis*

## Terminal

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1381	E	<b>Microscopic</b> larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx	- within normal limits - multinucleated, hepatocytes, mild - vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cyst, bilateral, minimal - within normal limits - fibrosis, minimal - within normal limits one of pair present - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1381	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1381	E	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, mild
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		uterus with cervix	- dilatation, gland/lumen, minimal
		vagina	- within normal limits
		Cause of Death	- pituitary tumor
1382	D	<b>Macroscopic</b> ears	- nodule, tan, right, present approximately 0.4 cm in diameter.
		lymph node, inguinal	- within normal limits draining node for mass a, left.
		pituitary gland	- enlarged, red, moderate
E - Euthanized <i>in extremis</i> D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - FEMALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1382	D	<b>Macroscopic</b> skin, subcutis	- mass, tan, mass a, left anogenital region, present approximately 2.5 cm in diameter.
1382	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - hyperplasia, focal medullary, bilateral, mild
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1382	D	<b>Microscopic</b> heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, inguinal lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic	- within normal limits - within normal limits - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - hyperplasia, bile duct, mild - within normal limits - within normal limits - within normal limits - dilatation, sinus, minimal - fibroadenoma, benign, primary, incidental, not cause of death corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1382	D	<b>Microscopic</b> nose, level a nose, level b nose, level c  nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - foreign material, mild plant. - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1382	D	<b>Microscopic</b> skin, subcutis  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix	- schwannoma, benign, primary, incidental, not cause of death corresponds to macroscopic observation (ears - nodule)  - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, minimal - metaplasia, squamous, minimal
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1382	D	<b>Microscopic</b> vagina Cause of Death	- within normal limits - undetermined
1383	D	<b>Macroscopic</b> lymph node, axillary  pituitary gland skin, subcutis	- within normal limits draining node for mass a, right. - enlarged, red, mild - mass, ulcerated, mass a, right axillary area, present corresponds to antemortem observation (mass 1 cannibalized/partially cannibalized) approximately 10.0 x 6.5 x 5.5 cm, tan. majority of skin covering mass appears to be cannibalized.
1383	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - hyperplasia, mixed, mild - hyperplasia, mixed, mild
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1383	D	<b>Microscopic</b> bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - pyelitis, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1383	D	<b>Microscopic</b> liver lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx	- focus of cellular alteration, basophilic, minimal - histiocytosis, alveolar, minimal - hyperplasia, lymphocyte/plasmacyte, medulla, mild - within normal limits - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1383	D	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, mild
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1383	D	<b>Microscopic</b> thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina  Cause of Death	- depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - granular cell tumor, benign, primary, incidental, not cause of death - mammary tumor
1384	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass c and mass f, right and mass d, mass e, left.
E - Euthanized <i>in extremis</i> D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - FEMALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1384	E	<b>Macroscopic</b> lymph node, inguinal	- not identified, bilateral, no grade draining node for mass a and mass g, left and mass b and mass h, right.
		lymph node, mandibular	- within normal limits draining node for mass i, right.
		pituitary gland	- enlarged, red, mild
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1384	E	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, black, mass b, right inguinal area, present corresponds to antemortem observation (mass 2) approximately 3.5 x 3.0 x 1.2 cm.</li> <li>- mass, red, mass d, left axillary area, present corresponds to antemortem observation (mass 4) approximately 1.5 cm in diameter.</li> <li>- mass, red, mass i, right lateral neck, present approximately 1.5 cm in diameter.</li> <li>- mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 1.5 cm in diameter.</li> <li>- mass, tan, mass c, right axillary area, present corresponds to antemortem observation (mass 3) approximately 1.0 cm in diameter.</li> <li>- mass, tan, mass e, left axillary area, present corresponds to antemortem observation (mass 5) approximately 2.5 x 2.0 x 1.0 cm.</li> <li>- mass, tan, mass g, left anogenital region, present approximately 3.5 x 2.0 x 1.0 cm.</li> <li>- mass, tan, mass h, right anogenital region, present approximately 3.0 x 2.0 x 1.3 cm.</li> <li>- mass, ulcerated, mass f, right axillary area, present corresponds to antemortem observation (mass 6) approximately 3.0 x 2.5 x 1.0 cm, red.</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1384	E	<b>Macroscopic</b> thymus	- small, severe
1384	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - hyperplasia, focal medullary, bilateral, mild
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), mild
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- hyperplasia, focal, unilateral, minimal
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1384	E	<b>Microscopic</b> kidneys	- hyperplasia, transitional cell, bilateral, minimal - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - pyelitis, unilateral, minimal
		lacrimal glands, exorbital	- within normal limits
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- within normal limits
		liver	- infiltration, mononuclear cell, minimal
		lung	- histiocytosis, alveolar, minimal
		lymph node, axillary	- within normal limits
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1384	E	<b>Microscopic</b> mammary gland	- adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b; skin, subcutis - mass c; skin, subcutis - mass d; skin, subcutis - mass e; skin, subcutis - mass f; skin, subcutis - mass g; skin, subcutis - mass h; skin, subcutis - mass i) - hyperplasia, lobular, minimal - degeneration, axonal/myelin, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits one of pair present
		pharynx	- within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1384	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1384	E	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, moderate corresponds to macroscopic observation (thymus - small)
		thyroid gland	- hyperplasia, epithelial cell, minimal - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		uterus with cervix	- dilatation, gland/lumen, minimal
		vagina	- within normal limits
		Cause of Death	- mammary tumor
1385	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass a, right.
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1385	E	<b>Macroscopic</b> skin, subcutis	- mass, ulcerated, mass a, right axillary area, present corresponds to antemortem observation (hair sparse scabbed area mass 1) approximately 6.0 cm in diameter, tan.
1385	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - hyperplasia, focal cortical, unilateral, minimal one medulla present - within normal limits - within normal limits - angiectasis, mild - within normal limits - within normal limits - astrocytoma, malignant, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1385	E	<b>Microscopic</b> eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - within normal limits - within normal limits - mineralization, pelvic, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, mild - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1385	E	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- degeneration/necrosis, myofiber, minimal
		skin	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1385	E	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - hyperplasia, follicular cell, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1385	E	<b>Microscopic</b> Cause of Death	- mammary tumor
1386	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1386	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1386	E	<b>Microscopic</b> harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c	- within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, eosinophilic, minimal - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1386	E	<b>Microscopic</b> nose, level d ovaries oviducts pancreas  parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum	- within normal limits - cyst, unilateral, minimal - within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1386	E	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1387	E	<b>Macroscopic</b> adrenal glands mammary gland pituitary gland	- enlarged, right, moderate - swollen/thickened, cervical, inguinal, mild - enlarged, severe
1387	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1387	E	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic	- within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, unilateral, minimal - pyelitis, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits - hyperplasia, lobular, mild corresponds to macroscopic observation (mammary gland - swollen/thickened) - degeneration, axonal/myelin, minimal

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1387	E	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1387	E	<b>Microscopic</b> small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1388	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1388	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), moderate
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1388	E	<b>Microscopic</b> kidneys	- mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - pyelitis, unilateral, minimal
		lacrimal glands, exorbital	- within normal limits
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- within normal limits
		liver	- hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - vacuolation, periportal, mild
		lung	- infiltration, lymphoid, perivascular, mild
		lymph node, mandibular	- erythrocytosis/erythrophagocytosis, sinus, mild
		lymph node, mesenteric	- within normal limits
		mammary gland	- hyperplasia, lobular, minimal
		nerve, sciatic	- degeneration, axonal/myelin, minimal
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1388	E	<b>Microscopic</b> nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical	- within normal limits - within normal limits - within normal limits - fibrosis, minimal - not examined - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1388	E	<b>Microscopic</b> spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1389	S	<b>Macroscopic</b> liver	- focus/foci, red, multiple lobes, mild

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1389	S	<b>Macroscopic</b> lymph node, inguinal  skin, subcutis	- not identified, bilateral, no grade draining node for mass a and b. - mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 5.0 cm in diameter. - mass, tan, mass b, right inguinal area, present corresponds to antemortem observation (swelling) approximately 1.0 cm in diameter. - enlarged, horn, mild
1389	S	uterus with cervix <b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1389	S	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	- within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1389	S	<b>Microscopic</b> liver	- degeneration, cystic, focal, minimal - dilatation, cystic, bile ducts, mild - focus of cellular alteration, basophilic, mild - hyperplasia, bile duct, mild - vacuolation, periportal, minimal
		lung	- inflammation, subacute/chronic, minimal
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
		mammary gland	- fibroadenoma, benign, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b)
		nerve, sciatic	- hyperplasia, lobular, mild
		nose, level a	- degeneration, axonal/myelin, minimal
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1389	S	<b>Microscopic</b> pancreas parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular	- within normal limits - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1389	S	<b>Microscopic</b> stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix  vagina non-correlated macro observation	- within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, lymphoid, medulla, mild - hyperplasia, c-cell, focal, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild corresponds to macroscopic observation (uterus with cervix - enlarged) - within normal limits - liver - focus/foci, red
1390	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass b, right.

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1390	E	<b>Macroscopic</b> lymph node, inguinal  lymph node, mandibular  pituitary gland skin, subcutis   spleen thymus vagina	- not identified, left, no grade draining node for mass a. - within normal limits draining node for mass c, left. - enlarged, red, mild - mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 5.0 x 5.0 x 3.0 cm. - mass, tan, mass b, right axillary area, present corresponds to antemortem observation (mass 2) approximately 2.0 cm in diameter. - mass, tan, mass c, ventral neck, left, present corresponds to antemortem observation (mass 3) approximately 4.0 x 2.5 x 2.0 cm. - enlarged, mild - small, severe - prolapse, mild corresponds to antemortem observation (reproductive tract prolapsed)
1390	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1390	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital	- within normal limits - hyperplasia, granulocytic, mild - hyperplasia, granulocytic, mild - within normal limits - within normal limits - carcinoma, pars distalis, malignant, secondary - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - within normal limits - within normal limits - hydronephrosis, unilateral, mild - hyperplasia, transitional cell, unilateral, minimal - mineralization, pelvic, unilateral, mild - nephropathy, chronic progressive, bilateral, minimal - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1390	E	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland   nerve, sciatic nose, level a nose, level b nose, level c	- within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits - abscess, severe corresponds to macroscopic observation (skin, subcutis - mass b) - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass c) - hyperplasia, lobular, moderate - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1390	E	<b>Microscopic</b> nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum	- within normal limits - cyst, unilateral, minimal - within normal limits - atrophy, acinar, minimal - within normal limits - within normal limits - carcinoma, pars distalis, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosarcoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1390	E	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen  stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina  Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, moderate corresponds to macroscopic observation (spleen - enlarged) - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate corresponds to macroscopic observation (thymus - small) - within normal limits - inflammation, acute, minimal - within normal limits - dilatation, unilateral, mild - within normal limits - hyperplasia, cervical fibromuscular, moderate - hyperplasia, fibromuscular, moderate - prolapse, no grade corresponds to macroscopic observation (vagina - prolapse) - vagina; prolapse; no grade

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1391	E	<b>Macroscopic</b> all tissues	- within normal limits
1391	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - hyperplasia, focal cortical, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- hemorrhage, moderate
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, minimal
		joint, tibiofemoral	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1391	E	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c	- hyperplasia, transitional cell, unilateral, minimal - mineralization, pelvic, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1391	E	<b>Microscopic</b> nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	 - within normal limits - cyst, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1391	E	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, minimal - hyperplasia, c-cell, focal, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1392	S	<b>Macroscopic</b> mammary gland	- swollen/thickened, tan, generalized, mild corresponds to antemortem observation (swelling)
1392	S	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild

S - Scheduled necropsy  
E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1392	S	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, mild - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1392	S	<b>Microscopic</b> large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- within normal limits</li> <li>- dilatation, cystic, bile ducts, minimal</li> <li>- focus of cellular alteration, basophilic, mild</li> <li>- hyperplasia, bile duct, minimal</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- adenoma, benign, primary, incidental, not cause of death very small, on slide 18-1.</li> <li>- fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (mammary gland - swollen/thickened) slide 18-1.</li> <li>- hyperplasia, lobular, mild corresponds to macroscopic observation (mammary gland - swollen/thickened)</li> <li>- degeneration, axonal/myelin, minimal</li> <li>- inflammation, minimal</li> </ul>
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1392	S	<b>Microscopic</b> nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1392	S	<b>Microscopic</b> spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina	- within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, mild - hyperplasia, c-cell, focal, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild - within normal limits
1393	E	<b>Macroscopic</b> adrenal glands	- enlarged, right, mild

S - Scheduled necropsy  
E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1393	E	<b>Macroscopic</b> bone, mandible	- mass, ulcerated, mass b, left, present corresponds to antemortem observation (mass 2) approximately 4.5 x 2.0 x 2.5 cm, tan.
		lymph node, inguinal	- not identified, left, no grade draining node for mass a.
		lymph node, mandibular	- within normal limits draining node for mass b, left.
		pituitary gland	- enlarged, moderate
		skin, subcutis	- mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 5.5 x 4.5 x 2.5 cm.
		thymus	- small, moderate
		tooth/teeth	- absent/broken/malocclusion/overgrown, no grade corresponds to antemortem observation (malocclusion)
1393	E	uterus with cervix <b>Microscopic</b> adrenal glands	- enlarged, horn, mild  - angiectasis/cystic degeneration, focal cortical, bilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged)

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1393	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	- within normal limits - hyperplasia, granulocytic, mild - hyperplasia, granulocytic, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - hyperplasia, transitional cell, unilateral, mild - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, unilateral, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1393	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries	- within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, mild - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - inflammation, acute, minimal - within normal limits - within normal limits - within normal limits - fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1393	E	<b>Microscopic</b> oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- within normal limits - atrophy, acinar, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - atrophy, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1393	E	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix  vagina zymbal's gland  Cause of Death	- within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe corresponds to macroscopic observation (thymus - small) - hyperplasia, c-cell, focal, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, moderate corresponds to macroscopic observation (uterus with cervix - enlarged) - within normal limits - carcinoma, sebaceous cell, malignant, unilateral, primary, mortality-independent corresponds to macroscopic observation (bone, mandible - mass b) - zymbals gland tumor

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1394	E	<b>Macroscopic</b> lymph node, axillary  lymph node, mandibular  pituitary gland skin, subcutis	- within normal limits draining node for mass b, right. - within normal limits draining node for mass a, right. - enlarged, severe - mass, tan, mass a, cervical, right, present corresponds to antemortem observation (mass 1) approximately 1.5 cm in diameter. - mass, tan, mass b, right axillary area, present corresponds to antemortem observation (mass 2) approximately 1.5 cm in diameter.
1394	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal - hyperplasia, focal cortical, unilateral, mild - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

## Terminal

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1394	E	<b>Microscopic</b> liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland   nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries	- focus of cellular alteration, basophilic, mild - hyperplasia, bile duct, minimal - granuloma, minimal - within normal limits - erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits - adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b) - adenoma, benign, primary, incidental, not cause of death slide 18. - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, sex-cord/stromal, bilateral, minimal

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1394	E	<b>Microscopic</b> oviducts pancreas  parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar	- within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1394	E	<b>Microscopic</b> spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, epithelial cell, mild - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - hyperplasia, c-cell, focal, unilateral, mild - within normal limits - within normal limits - dilatation, unilateral, mild - within normal limits - within normal limits - within normal limits - pituitary tumor
1395	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, moderate

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1395	E	<b>Macroscopic</b> skin	- hair sparse, dorsal cervical region, dorsal thoracic region, mild corresponds to antemortem observation (hair sparse)
1395	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), moderate
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1395	E	<b>Microscopic</b> joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts	- within normal limits - mineralization, pelvic, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - within normal limits - erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits - hyperplasia, lobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1395	E	<b>Microscopic</b> pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- within normal limits - not examined - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - alopecia/hypotrichosis, mild corresponds to macroscopic observation (skin - hair sparse) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1395	E	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - not examined - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1396	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1396	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, mild

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1396	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, unilateral, minimal - pyelitis, bilateral, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1396	E	<b>Microscopic</b> large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands pharynx	- within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - vacuolation, periportal, moderate - histiocytosis, alveolar, minimal - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - cyst, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1396	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- degeneration/necrosis, myofiber, minimal
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- hyperplasia, epithelial, nonglandular, moderate - inflammation, mild

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1396	E	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder  uterus with cervix  vagina Cause of Death	- depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, simple transitional cell, moderate - inflammation, minimal - granular cell tumor, benign, primary, incidental, not cause of death - hyperplasia, squamous cell, mild - within normal limits - pituitary tumor
1397	D	<b>Macroscopic</b> lymph node, inguinal  pituitary gland	- not identified, right, no grade draining node for mass a. - enlarged, red, severe
E - Euthanized <i>in extremis</i> D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1397	D	<b>Macroscopic</b> skin  skin, subcutis	- abrasion/scab, red, right axillary area, mild corresponds to antemortem observation (scabbed area hair sparse) - mass, firm, mass a, right anogenital region, present corresponds to antemortem observation (swelling) approximately 3.3 x 2.8 x 1.8 cm, tan.
1397	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina	- hyperplasia, focal cortical, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis

D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1397	D	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - dilatation, tubular, bilateral, minimal - mineralization, pelvic, bilateral, minimal - mineralization, tubular, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - hyperplasia, bile duct, minimal - vacuolation, periportal, minimal - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1397	D	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- not examined
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits

D - Died on Study

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1397	D	<b>Microscopic</b> salivary gland, sublingual skeletal muscle, biceps femoris skin  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder	- within normal limits - within normal limits - adenoma, basal cell, benign, primary, mortality-independent corresponds to macroscopic observation (skin - abrasion/scab) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1397	D	<b>Microscopic</b> uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - pituitary tumor
1398	E	<b>Macroscopic</b> lymph node, axillary  mammary gland pituitary gland skin, subcutis	- within normal limits draining node for mass a, left. - swollen/thickened, tan, generalized, moderate - enlarged, red, moderate - mass, tan, mass a, left axillary area, present corresponds to antemortem observation (mass 1) approximately 3.5 cm in diameter. - irregular surface, tan, mild
1398	E	stomach, nonglandular <b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate - hyperplasia, focal medullary, bilateral, mild
E - Euthanized <i>in extremis</i> D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1398	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - within normal limits - within normal limits - mineralization, pelvic, bilateral, minimal - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1398	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary  lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- focus of cellular alteration, basophilic, minimal</li> <li>- hyperplasia, bile duct, minimal</li> <li>- infiltration/inflammation, mixed cell, minimal</li> <li>- vacuolation, centrilobular, moderate</li> <li>- histiocytosis, alveolar, minimal</li> <li>- not examined</li> <li>- misidentified tissue</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- adenocarcinoma, malignant, primary, incidental, not cause of death</li> <li>- small, slide 18.</li> <li>- fibroadenoma, benign, primary, mortality-independent</li> <li>- corresponds to macroscopic observation (skin, subcutis - mass a)</li> <li>- hyperplasia, lobular, moderate</li> <li>- corresponds to macroscopic observation (mammary gland - swollen/thickened)</li> <li>- degeneration, axonal/myelin, minimal</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1398	E	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - within normal limits - within normal limits - cyst, unilateral, mild - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1398	E	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  thymus  thyroid gland tongue trachea ureters urinary bladder	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - erosion/ulcer, mild - hyperplasia, epithelial, nonglandular, moderate corresponds to macroscopic observation (stomach, nonglandular - irregular surface) - inflammation, mild - depletion, lymphoid, generalized, severe - hyperplasia, epithelial cell, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u>			
1398	E	<b>Microscopic</b> uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - pituitary tumor
1399	E	<b>Macroscopic</b> skin	- absent portion/cannibalized, left hindleg/limb, left ventral abdomen, no grade corresponds to antemortem observation (laceration)
1399	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum	- angiectasis/cystic degeneration, focal cortical, bilateral, mild one medulla present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1399	E	<b>Microscopic</b> brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - mineralization, tubular, unilateral, minimal  - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1399	E	<b>Microscopic</b> lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas parathyroid glands  pharynx pituitary gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin	- within normal limits - hyperplasia, lobular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1399	E	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - loss of hindlimb function, cause undetermined.

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1400	E	<b>Macroscopic</b> adrenal glands kidneys lung with bronchi lymph node, inguinal  pituitary gland skin  skin, subcutis	- enlarged, left, mild - focus/foci, tan, bilateral, mild - focus/foci, tan, multiple lobes, mild - not identified, left, no grade draining node for mass b. draining node for mass c, right. - enlarged, red, severe - abrasion/scab, ventral neck, mild corresponds to antemortem observation (scabbed area) - mass, tan, mass b, left inguinal area, present corresponds to antemortem observation (mass 2) approximately 2.0 cm in diameter. - mass, tan, mass c, right inguinal area, present corresponds to antemortem observation (mass 3) approximately 3.0 cm in diameter. - enlarged, red, horn, mild
1400	E	uterus with cervix <b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, unilateral, moderate corresponds to macroscopic observation (adrenal glands - enlarged)

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1400	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, mild - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1400	E	<b>Microscopic</b> large intestine, rectum larynx liver  lung  lymph node, inguinal lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - hyperplasia, bile duct, minimal - vacuolation, periportal, minimal - histiocytosis, alveolar, mild corresponds to macroscopic observation (lung with bronchi - focus/foci, tan) - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1400	E	<b>Microscopic</b> mammary gland	- adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin - abrasion/scab; skin, subcutis - mass b; skin, subcutis - mass c) slide 18-1, 26-1, and 26-2. - hyperplasia, lobular, mild - degeneration, axonal/myelin, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits one of pair present
		pharynx	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1400	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0 mg/kg/day</u> 1400	E	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, moderate
			- hyperplasia, epithelial cell, minimal
		thyroid gland	- within normal limits
		tongue	- hyperplasia, squamous cell, mild
			- inflammation, subacute/chronic, mild
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		uterus with cervix	- polyp, stromal, benign, primary, incidental, not cause of death corresponds to macroscopic observation (uterus with cervix - enlarged)
		vagina	- within normal limits
		non-correlated macro observation	- kidneys - focus/foci, tan
		Cause of Death	- pituitary tumor
<u>1 mg/kg/day</u> 1411	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1411	E	<b>Macroscopic</b> thymus	- small, mild
1411	E	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, bilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), moderate
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1411	E	<b>Microscopic</b> kidneys	- mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - pyelitis, unilateral, minimal
		lacrimal glands, exorbital	- within normal limits
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- within normal limits
		liver	- within normal limits
		lung	- within normal limits
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
		mammary gland	- hyperplasia, lobular, minimal
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1411	E	<b>Microscopic</b> oviducts pancreas parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- within normal limits - within normal limits - not examined - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1411	E	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe corresponds to macroscopic observation (thymus - small) - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1412	E	<b>Macroscopic</b> lymph node, inguinal	- not identified, bilateral, no grade draining node for mass a and mass b, right and mass c, left.

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1412	E	<b>Macroscopic</b> mammary gland pituitary gland skin, subcutis	<ul style="list-style-type: none"> <li>- swollen/thickened, tan, mild</li> <li>- enlarged, red, mild</li> <li>- mass, tan, mass b, right inguinal area, present corresponds to antemortem observation (mass 2) approximately 5.0 x 5.0 x 1.0 cm.</li> <li>- mass, tan, mass c, left inguinal area, present corresponds to antemortem observation (mass 3) approximately 8.0 x 9.0 x 4.0 cm.</li> <li>- mass, ulcerated, mass a, anogenital region, present corresponds to antemortem observation (mass 1 hair sparse) approximately 5.0 x 5.0 x 3.0 cm, tan.</li> </ul>
1412	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum	<ul style="list-style-type: none"> <li>- angiectasis/cystic degeneration, focal cortical, bilateral, mild</li> <li>- within normal limits</li> <li>- hyperplasia, granulocytic, mild</li> <li>- hyperplasia, granulocytic, minimal</li> <li>- within normal limits</li> <li>- within normal limits</li> </ul>

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1412	E	<b>Microscopic</b> brain esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - hematopoiesis, extramedullary, minimal - vacuolation, periportal, minimal
E - Euthanized <i>in extremis</i>			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1412	E	<b>Microscopic</b> lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- adenocarcinoma, malignant, multiple, primary, mortality-independent</li> <li>- corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b)</li> <li>- hyperplasia, lobular, moderate</li> <li>- corresponds to macroscopic observation (mammary gland - swollen/thickened)</li> <li>- degeneration, axonal/myelin, minimal</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- cyst, unilateral, minimal</li> <li>- within normal limits</li> </ul>

E - Euthanized *in extremis*



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1412	E	<b>Microscopic</b> pancreas	- adenoma, islet cell, benign, primary, incidental, not cause of death
		parathyroid glands	- atrophy, acinar, mild - within normal limits one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		skin, subcutis	- fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass c)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1412	E	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular thymus  thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, mild - within normal limits - within normal limits - depletion, lymphoid, generalized, mild - hyperplasia, epithelial cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mammary tumor

E - Euthanized *in extremis*

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1413	D	<b>Macroscopic</b> adrenal glands lymph node, axillary  lymph node, inguinal  mammary gland pituitary gland skin, subcutis	<ul style="list-style-type: none"> <li>- enlarged, left, mild</li> <li>- within normal limits</li> <li>- draining node for mass a, left and draining node for mass b, right.</li> <li>- not identified, right, no grade</li> <li>- draining node for mass c.</li> <li>- swollen/thickened, tan, generalized, moderate</li> <li>- enlarged, moderate</li> <li>- mass, tan, mass a, left axillary area, present corresponds to antemortem observation (mass 1) approximately 4.0 x 4.0 x 1.0 cm.</li> <li>- mass, tan, mass b, right axillary area, present corresponds to antemortem observation (hair sparse mass 2) approximately 5.0 x 3.0 x 1.0 cm.</li> <li>- mass, tan, mass c, right inguinal area, present corresponds to antemortem observation (nodule) approximately 4.5 x 3.0 x 1.0 cm.</li> </ul>
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1413	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, unilateral, severe corresponds to macroscopic observation (adrenal glands - enlarged)
		aorta	- within normal limits
		bone marrow, femur	- hyperplasia, granulocytic, mild
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), moderate - hemorrhage, minimal
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, minimal
		joint, tibiofemoral	- within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - FEMALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1413	D	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric	- mineralization, pelvic, unilateral, minimal - mineralization, tubular, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - FEMALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1413	D	<b>Microscopic</b> mammary gland	<ul style="list-style-type: none"> <li>- adenocarcinoma, malignant, multiple, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b)</li> <li>- fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass c)</li> <li>- hyperplasia, lobular, moderate corresponds to macroscopic observation (mammary gland - swollen/thickened)</li> </ul>
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits one of pair present
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1413	D	<b>Microscopic</b> pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular	- within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1413	D	<b>Microscopic</b> thymus thyroid gland  tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- depletion, lymphoid, generalized, moderate - carcinoma, follicular cell, malignant, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild - within normal limits - pituitary tumor
1414	D	<b>Macroscopic</b> lymph node, axillary  pituitary gland skin, subcutis	- within normal limits draining node for mass a, right. - enlarged, red, mild - mass, tan, mass a, right axillary area, present corresponds to antemortem observation (swelling) approximately 1.0 cm in diameter.
D - Died on Study			



Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1414	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- not examined autolysis too severe for diagnosis
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, minimal
		joint, tibiofemoral	- within normal limits
		kidneys	- mineralization, pelvic, bilateral, minimal - mineralization, tubular, unilateral, minimal
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1414	D	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d ovaries oviducts pancreas	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, lobular, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1414	D	<b>Microscopic</b> parathyroid glands pharynx pituitary gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- not examined - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - cyst, keratin, minimal - fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1414	D	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular thymus thyroid gland tongue trachea ureters urinary bladder uterus with cervix vagina Cause of Death	- within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
1415	D	<b>Macroscopic</b> lymph node, axillary  mammary gland pituitary gland	- within normal limits draining node for mass a, right. - swollen/thickened, tan, generalized, mild - enlarged, red, severe
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1415	D	<b>Macroscopic</b> skin, subcutis	- mass, red, mass a, right axillary area, present corresponds to antemortem observation (mass 1) approximately 4.0 cm in diameter.
1415	D	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain esophagus eyes eyes, optic nerves eyes, retina	- angiectasis/cystic degeneration, focal cortical, bilateral, moderate one medulla present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1415	D	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys  lacrimial glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - mineralization, tubular, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Animal Listing - FEMALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1415	D	<b>Microscopic</b> mammary gland	- fibroadenoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, lobular, mild corresponds to macroscopic observation (mammary gland - swollen/thickened)
		nerve, sciatic	- degeneration, axonal/myelin, minimal
		nose, level a	- exudate, nasal passage, mild - foreign material, minimal plant.
		nose, level b	- exudate, nasal passage, minimal - foreign material, minimal plant.
		nose, level c	- exudate, nasal passage, mild
		nose, level d	- within normal limits
		ovaries	- within normal limits
		oviducts	- within normal limits
		pancreas	- atrophy, acinar, mild
		parathyroid glands	- within normal limits one of pair present
D - Died on Study			